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Predictive power of blood urea nitrogen and albumin ratio for mortality in acute ischemic stroke

Blood urea nitrogen and albumin ratio for mortality in acute ischemic stroke

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Abstract
Aim: Globally, acute ischemic stroke (AIS) is one of the leading causes of death and permanent disability. The ratio of blood urea nitrogen to serum albumin (BAR) is a prognostic biomarker that combines two important determinants and has excellent predictive potential for mortality in critically sick patients. This study investigated the relationship between BAR and in-hospital mortality in AIS patients diagnosed in the emergency department (ED).
Material and Methods: A retrospective analysis of data of AIS patients aged 18 and older who presented to our emergency department during the study period was performed. Data were acquired from the hospital's computerized information system. Each discriminant mortality cut-off value was evaluated using the receiver operating characteristic (ROC) curve and area under the curve (AUC).
Results: The study included a total of 300 patients with a mean age of 67.1±14.4 years; 156 (52%) of them were male. The mean length of stay in the hospital was found to be 7 days, and 67 patients were transferred to the intensive care units. Fifteen patients (5%) died during their follow-up in the hospital. As a result of the ROC analysis of BAR to predict the presence of in-hospital mortality, the AUC value was determined as 0.756 (95% confidence interval: 0.704-0.804), the Youden index as 0.47, and the p-value as 0.001. At a cut-off value of >4.21, BAR had a sensitivity of 93.3%, specificity of 54.4%, positive predictive value of 9.7, and negative predictive value of 99.4 in determining the presence of in-hospital mortality.
Discussion: BAR is a simple and useful in-hospital mortality predictor in patients with AIS.

Keywords
Stroke, Albumin, Blood Urea Nitrogen, Mortality

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Introduction

Globally, stroke is among the most crucial cause of mortality and long-term disability (available at: https://www.cdc.gov/stroke/facts.htm). In the USA, 795,000 adults die or become disabled due to stroke every year [1], and approximately 77% of stroke cases occur for the first time and 23% are recurrent [2]. Stroke ranks as the fifth leading cause of death in United States, causing approximately 140,000 deaths annually, with an estimated annual effect on health resources (lost work days, healthcare, and treatment) of $46 billion. [1].

The early prediction of poor outcomes following cerebral ischemia might improve decision-making steps, such as early admission to dedicated stroke units, and hence aid in patient management. However, the outcomes of stroke remain difficult to predict. Therefore, various studies have been undertaken to investigate the effects of various scoring systems and blood parameters on the prognosis of stroke [3-5].

The ratio of blood urea nitrogen (BUN) to serum albumin (BAR) is a recently found prognostic biomarker that combines two essential markers (BUN and albumin) and accurately predicts the mortality of critically ill patients [6,7]. BUN is a measure of dehydration in patients, and increased BUN levels have been connected with in-hospital mortality among acute ischemic stroke patients (AIS) [8]. As a negative acute phase reactant, albumin is an important inflammatory marker that plays a role in maintaining osmotic pressure and transporting important molecules in the body [9]. Studies have shown that a low serum albumin level is linked to a negative outcome for people with AIS [10].

This study examined the relationship between BAR and in-hospital mortality in individuals diagnosed with AIS who presented to the emergency department.

Material and Methods

Study design

A tertiary-level hospital's emergency department was the setting for this retrospective, observational study. The study was conducted between January 1, 2020 and June 1, 2021. Due to the retrospective nature of the investigation, the institutional review board approved the analysis and waived the need for written informed consent (Ethics Committee ruling number: HNEAH-KAEK 2022/72, date: 04.04.2022).

Selection of patients

Patients diagnosed with AIS were identified among individuals over 18 years old who presented to the emergency department during the study period, using the International Classification of Diseases 10th Revision (ICD-10) codes. Patients with a diagnosis other than AIS, those with deficiencies in BUN and/or albumin, those referred from another hospital, and those that died at or were discharged from the emergency were excluded from the research.

Data collection and outcome measurement

The following data were collected by screening each patient's electronic medical records: age, gender, vital parameters (systolic-diastolic blood pressures, body temperature, and pulse), laboratory parameters, including BUN and albumin, in-hospital mortality, length of hospital stay and admission to the intensive care unit. If an eligible patient presented to the emergency department more than once during the study period, only the data belonging to the first visit were included in the analysis. BAR was determined by dividing the BUN level by the albumin level. The data were entered into an Excel database (Microsoft Corporation, Richmond, WA) and examined by the first researcher. Following analysis of the data, the other researcher made recommendations for enhancing quality. The primary outcome of the study was in-hospital mortality due to all-causes.

Statistical Analysis

Statistical analyses were carried out using IBM SPSS Statistics version 26.0 (SPSS Inc., Chicago, IL, USA) and MedCalc Statistical Software version 19.0.6 (MedCalc Software bvba, Ostend, Belgium). The Chi-square and Mann-Whitney U tests were used for the analysis of categorical and continuous data, respectively. Continuous data were reported as median and interquartile range values. Categorical data were given as frequency and percentages. A p-value that was less than 0.05 was used to indicate statistical significance. The receiver operating characteristic (ROC) analysis was performed using the DeLong method to assess the prognostic performance of BAR. The area under the curve (AUC) was calculated to evaluate the prognostic performance of BAR. Lastly, a Youden's J index (YJI) calculation was conducted for sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and the cut-off value at which AUC was the highest [11].

Results

The study included 300 patients with a mean age of 67.1 ± 14.4 years. There were 156 men and 144 women among the patients. Sixty-seven patients were taken to the hospital's intensive care units. The mean duration of hospital stay was found to be 7 days. Fifteen patients (5%) died during their follow-up in the hospital.

Table 1 shows the characteristics of the patients included in the study and some laboratory parameters.

The patients were separated as survivors and non-survivors, and their various characteristics were compared (Table 2). When various laboratory values were compared, it was determined that the mean values of BUN, creatinine, C-reactive protein and BAR were statistically higher in the group of non-survivors than the group of survivors (Table 2).

As a result of the ROC analysis of BAR in the prediction of in-hospital mortality, the AUC value was determined as 0.756

Table 1. Baseline characteristics of the patients

Variables	Min	Max	Mean Number	Standard deviation Percentage
C-reactive protein (mg/dL)	0.35	150.79	11.96	23.42
Blood urea nitrogen (mg/dL)	1.00	76.00	19.91	10.65
Creatinine (mg/dL)	0.52	14.10	1.09	0.89
Albumin (g/dL)	2.67	41.00	4.19	2.17
Length of hospital stay (days)	1.00	70.00	7.08	7.90
ICU admission			67	22.3
In hospital mortality			15	5.0
BAR	0.24	22.41	5.00	3.03

PT: prothrombin time, Aptt: activated partial thromboplastin time, INR: international normalized ratio, ICU: intensive care unit, BAR: BUN/Albumin ratio

(95% confidence interval: 0.704-0.804), YJI as 0.47, and the p-value as 0.001. According to the statistical analysis, BAR had a statistically significant power in predicting the presence of in-hospital mortality (p=0.001). At a cut-off value of >4.21, BAR had 93.3% sensitivity, 54.4% specificity, 9.7 PPV, and 99.4 NPV in the prediction of mortality of AIS patients in the hospital.

Table 2. Comparison of the characteristics of the survivor and non-survivor

		Mean Median	Standard deviation IQR	p value
C-reactive protein (mg/dL)	Survivor	10.33 3.0	19.39 7.74	0.006
	Non-survivor	42.97 7.0	54.78 86.5	
Blood urea nitrogen (mg/dL)	Survivor	19.15 16.0	9.27 8.9	0.001
	Non-survivor	34.40 22.0	21.04 32.5	
Creatinine (mg/dL)	Survivor	1.07 0.88	0.89 0.37	0.013
	Non-survivor	1.46 1.22	0.87 0.67	
Albumin (g/dL)	Survivor	4.21 4.10	2.22 0.44	0.123
	Non-survivor	3.84 4.02	0.54 0.54	
Length of hospital stay (days)	Survivor	6.67 5.0	6.99 4.00	0.009
	Non-survivor	14.73 12.0	16.69 12.00	
BAR	Survivor	4.76 4.09	2.54 2.41	0.001
	Non-survivor	9.56 5.87	6.48 11.93	

PT: prothrombin time, Aptt: activated partial thromboplastin time, INR: international normalized ratio, ICU: intensive care unit, BAR: BUN/Albumin ratio

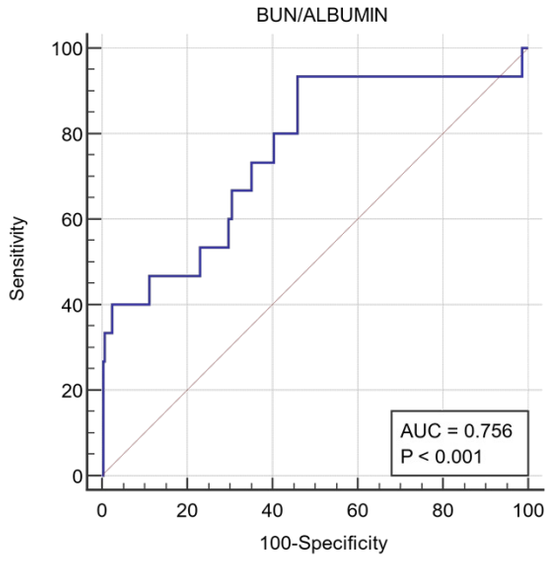

Figure 1. Receiver operating characteristic curve of the BUN-albumin ratio in predicting in-hospital mortality in patients with acute ischemic stroke

Discussion

In this study, we determined that BAR was a good predictor of in-hospital mortality in patients with AIS who presented to the emergency department. There are many studies in the literature investigating BAR as a prognostic predictor. BAR has been linked with negative outcomes in a variety of diseases and conditions, including pneumonia, bacteremia, and gastrointestinal bleeding [12-14]. Previous studies have shown that BAR can be defined as a prognostic marker for patients with AIS [15]. Although the relationship between high BUN levels and in-hospital mortality in patients with AIS has not yet been fully explained, there are some hypotheses concerning the underlying mechanism. First, a high BUN level at the time of hospital admission may be associated with hemodynamic deterioration, which is known to be associated with adverse outcomes in AIS patients [16]. Second, sympathetic nerve activity associated with urea reabsorption may lead to increased BUN after AIS, resulting in increased mortality [17]. Finally, BUN is a marker of hydration status. In case of dehydration, the blood flow to the organs decreases. Reduced blood flow to the brain may also lead to increased mortality in patients with AIS [18].

Albumin is a nutritional and hydration marker [19]. There are various mechanisms that explain the relationship between albumin and prognosis of AIS. It is known that albumin carries various drugs, free fatty acids, hormones, and amino acids in the blood. Thus, it can be suggested that albumin contributes to the improvement of brain perfusion by regulating the colloid osmotic pressure in the blood [20]. Lastly, there are also studies showing that hypoalbuminemia is associated with a high vascular thrombotic risk, emphasizing that albumin may play a role in inhibition of platelet aggregation [21].

Studies examining the correlation between elevated BUN and low albumin levels in predicting the prognosis of AIS can be found in the scientific literature. In a multi-center study, You et al. analyzed the data of 3,355 patients with AIS and concluded that elevated BUN levels at the time of admission to the hospital were independently associated with all-cause in-hospital mortality, but not with poor outcomes at discharge [8]. In a retrospective cohort study by Bae et al., the AUC value of BAR was found to be 0.687 in the prediction of in-hospital mortality in 1,164 patients with AIS [16]. In the same study, the cut-off value of BAR was calculated as 5.25, at which it had a sensitivity of 64.9% and specificity of 67.8% in determining the presence of in-hospital mortality. In our study, the AUC value of BAR was found to be 0.756 in the prediction of in-hospital-mortality in patients with AIS. At a cut-off value of >4.21, BAR had 93.3% sensitivity and 54.4% specificity in this prediction, which is consistent with the data reported in the literature.

This study had certain limitations. First, the results of a single-center study cannot be applied to the general population. Second, due to the retrospective design of the study, the patient data were obtained from the electronic medical records, which

Table 3. Predictive performance of the BUN-to-albumin ratio for mortality in patients with acute ischemic stroke

	AUC	Cut-off	Sensitivity	Specificity	+LR	-LR	PPV	NPV	Youden index	p value
BAR	0.756 (0.704-0.804)	>4.21	93.3 (68.1-99.8)	54.4 (48.1-59.9)	2.03	0.12	9.7	99.4	0.47	0.001

AUC: area under the curve, LR: likelihood ratio, PPV: positive predictive value, NPV: negative predictive value, BAR: BUN/Albumin ratio

may have led to the use of incomplete or erroneous data.

Conclusion

AIS continues to be a leading cause of death and disability worldwide. The admission of patients with AIS to the hospital begins at the emergency departments, and the early recognition of critically ill patients in this department contributes to their prognosis. In this study, we concluded that the BAR value of patients with AIS at the time of presentation to the emergency department had a good performance in predicting in-hospital mortality.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.

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Conflict of interest

None of the authors received any type of financial support that could be considered potential conflict of interest regarding the manuscript or its submission.

References

1. Virani SS, Alonso A, Benjamin EJ, Bittencourt MS, Callaway CW, Carson AP, et al. Heart disease and stroke statistics—2020 update: a report from the American Heart Association. Circulation. 2020; 141(9): e139–596.

2. Lackland DT, Roccella EJ, Deutsch AF, Fornage M, George MG, Howard G, et al. Factors influencing the decline in stroke mortality: a statement from the American Heart Association/American Stroke Association. Stroke 2014; 45(1): 315–53.

3. Ramiro L, Abraira L, Quintana M, García-Rodríguez P, Santamarina E, Álvarez-Sabín J, et al. Blood Biomarkers to Predict Long-Term Mortality after Ischemic Stroke. Life. 2021; 11(2): 135.

4. Sakal C, Ak R, Taşçı A, Kırkpantur E D, Ünal Akoğlu E, Cimilli Ozturk T. Admission blood lactate levels of patients diagnosed with cerebrovascular disease effects on short- and long-term mortality risk. International Journal of Clinical Practice. 2021; 75(8): 14161.

5. O'Donnell M J, Fang J, D'Uva C, Saposnik G, Gould L, McGrath E, et al. The PLAN score: a bedside prediction rule for death and severe disability following acute ischemic stroke. Arch Intern Med. 2012; 172(20): 1548-56.

6. Lin Z, Zhao Y, Xiao L, Qi C, Chen Q, Li Y. Blood urea nitrogen to serum albumin ratio as a new prognostic indicator in critical patients with chronic heart failure. ESC Heart Failure. 2022; 9(2): 1360-69.

7. Jihong F, Bin X. Blood urea nitrogen to serum albumin ratio independently predicts mortality in critically ill patients with acute pulmonary embolism. Clin Appl Thromb Hemost. 2021; 27. DOI: 10.1177/10760296211010241

8. You S, Zheng D, Zhong C, Wang X, Tang W, Sheng L, et al. Prognostic significance of blood urea nitrogen in acute ischemic stroke. Circ J. 2019; 82(2): 572-8.

9. Zhang Q, Lei Y, Wang Q, Jin Y, Fu R, Geng H, et al. Serum albumin level is associated with the recurrence of acute ischemic stroke. Am J Emerg Medicine. 2016; 34(9): 1812-16.

10. Babu MS, Kaul S, Dadheech S, Rajeshwar K, Jyothy A, Munshi A. Serum albumin levels in ischemic stroke and its subtypes: correlation with clinical outcome. Nutrition. 2013; 29: 872-5.

11. Fluss R, Faraggi D, Reiser B. Estimation of the Youden Index and its associated cutoff point. Biometrical Journal. 2005; 47(4): 458-72.

12. Ryu S, Oh SK, Cho SU, You Y, Park JS, Min JH, et al. Utility of the blood urea nitrogen to serum albumin ratio as a prognostic factor of mortality in aspiration pneumonia patients. Am J Emerg Med. 2021; 43: 175-9.

13. Zou XL, Feng D Y, Wu WB, Yang HL, Zhang TT. Blood urea nitrogen to serum albumin ratio independently predicts 30-day mortality and severity in patients with Escherichia coli bacteraemia. Medicina ClíNica. 2021; 157(5): 219-25.

14. Bae S J, Kim K, Yun S J, Lee S H. Predictive performance of blood urea nitrogen to serum albumin ratio in elderly patients with gastrointestinal bleeding. AmJ Emerg Med. 2021; 41; 152-7.

15. Bae S J, Lee S H, Yun S J, Kim K. Usefulness of the blood urea nitrogen-to-serum albumin ratio as a prognostic indicator of severity in acute ischemic stroke. Signa Vitae. 2021; 17(4): 163-70.

16. Baizabal-Carvallo JF, Alonso-Juarez M, Samson Y. Clinical deterioration following middle cerebral artery hemodynamic changes after intravenous thrombolysis for acute ischemic stroke. J Stroke Cerebrovasc Dis. 2014; 23(2): 254 - 8.

17. Erdur H, Scheitz JF, Grittner U, Laufs U, Endres M, Nolte CH. Heart rate on admission independently predicts in-hospital mortality in acute ischemic stroke patients. Int J Cardiol. 2014; 176(1): 206 - 10.

18. Aronson D, Mittleman MA, Burger AJ. Elevated blood urea nitrogen level as a predictor of mortality in patients admitted for decompensated heart failure. Am J Med. 2004; 116(7): 466-73.

19. Gerasimos Panagiotis M, Issaris V, Papavasileiou V. Blood urea nitrogen to albumin ratio as a predictive factor for pneumonia: a meta-analysis. Respiratory Medicine and Research. 2022; 100886.

20. Kanaiyalal DP, Sharma SS, Nilanjan Roy N. Current perspectives on potential role of albumin in neuroprotection. Reviews in the Neurosciences. 2011; 355-63.

21. Aksu K, Donmez ., Keser G. Inflammation-induced thrombosis: mechanisms, disease associations and management. Curr Pharm Des. 2012: 18(11)Ş 1478-93.

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